and transported to the interstitium was enhanced in diabetics compared to controls. The overexpression of CAV-1 and eNOS was also documented in diabetic groups suggesting enhanced transendothelial transport and hyperpermeability of these capillaries. In some cases immediate insulin replacement prevented the development of diabetes-related region-specific alterations.

These results indicate a close relationship between the segment-specific diabetic nitrergic neuropathy and vascular dysfunction of mesenterial capillaries running in the vicinity of myenteric plexus in the gut. Our data provide morphological, functional and molecular evidence that the endothelial cells of these vessels are direct targets of diabetic damage. We suggest therefore that these endothelial cells are potential therapeutic targets to prevent the development of the nitrergic neuropathy and the gut motility disorders in diabetic patients.

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Molecular characterization of the computationally predicted *miR-282* microRNA gene of *Drosophila melanogaster*

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MicroRNAs have been discovered as a new type of regulatory genes whose transcripts are marked by a representative intermedier form, the hairpin structure. Due to this typical secondary structure and the advanced bioinformatic methods, hundreds of new miRNA genes have been identified in animals, plants and even viruses. Hundreds of target genes for every single miRNA also have been predicted. In this way, a huge amount of data has been generated, which is waiting for interpretation and experimental confirmation.

MicroRNAs (miRNAs) are ~22 nucleotide long, single-stranded regulatory RNAs that bind to complementary sequences in the three prime untranslated regions of target mRNAs thereby, negatively regulating (by transcript degradation and translational suppression) the target genes. Although a significant group of miRNA genes is found in the introns or sometimes in exons of protein and non-protein coding genes, most microRNA genes lie in intergenic regions and contain their own promoter and regulatory components. MicroRNA primary transcripts (pri-miRNAs) are synthesized by RNA polymerase II. In this way, pri-miRNAs which range couple thousands of nucleotides in length have 5' m7G cap structure and usually subjected to polyadenylation in their 3' end. However the functional analyses are still in their infancy because they are hampered primarily by redundancy among miRNA genes occurring when different miRNAs share the same 5' seed sequence or their target(s) and if they are coexpressed. Moreover, most miRNA mutants show subtle or low-penetrance defects that may be difficult to identify. As a consequence, in only few cases can lead the lack of miRNA function to robust phenotypes. Despite of these findings, it has become clear today that miRNAs are required for the fine tuning of the regulation of sometimes very complex mechanisms and participate in the regulation of almost every biological processes investigated so far.

While in the fruit fly (*Drosophila melanogaster*) 176 miRNAs has been computationally predicted to date (miRBase release 16), the real target mRNAs and biological function have been assigned to only a dozen of them. We characterized a miRNA gene, *mir-282* of *Drosophila melanogaster* which is evolutionary conserved among insects. The *mir-282* gene is located on the third chromosome within a 13.9 kb genomic region devoid of any protein coding genes and our data strongly suggest an independent *mir-282* gene whose primary transcript has a distinct 5' start with a CAP and a few alternative 3' ends with polyA tail. We have determined the correct size of the pre- and mature *mir-282*. We found that the *mir-282* locus encodes a functional transcript which influences viability, longevity and egg production in Drosophila, most likely through the regulation of cAMP level at pupal stage.

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Neuroprotection with novel KYNA-amide

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Acute protection and the recovery of neurons from cerebral ischemic insults of whatever nature give rise to the main drive in the development of neuroprotective strategies.

The most widely accepted concept relating to ischemic brain damage is the concept of excitotoxicty.

Treatment with N-methyl-D-aspartate receptor antagonists is a widely accepted method with which to stop the advance of excitotoxic processes and concomitant neuronal death. From a clinical aspect, competitive glycine- and polyamine-site antagonists with relatively low affinity and moderate side-effects are taken into account. Endogenous kynurenic acid (KYNA) acts as an antagonist on the obligatory co-

agonist glycine site, and has long been at the focus of neuroprotective trials. Unfortunately, KYNA is barely able to cross the blood-brain barrier. Accordingly, the development and synthesis of KYNA analogs which can readily cross the BBB have been at the focus of research interest with the aim of neuroprotection.

A novel KYNA analog, 2-(2-N,N-dimethylaminoethylamine-1-carbonyl)-1H-quinolin-4-one hydrochloride (Patent Application No: 104448-1998/Ky/me), recently proved to be neuroactive in several experimental paradigms. The analog effectively reduced c-fos and nNOS activation in an experimental animal model of migraine, effects interpreted as due to NMDA blockade. Moreover, in an *in vitro* comparative electrophysiological study, this compound was found to have the same neuromodulatory attributes as KYNA. NMDA antagonism was also acknowledged. 1 mmol of the analog administered i.p. effectively reduces the amplitudes of hippocampal population spikes. Regarding these properties, we estimated the neuroprotective capability of a novel kynurenic acid analog in transient global forebrain ischemia, measuring the rate of hippocampal CA1 pyramidal cell loss and the preservation of long-term potentiation at Schaffer collateral-CA1 synapses.

The neuroprotective potential was reflected by a significantly diminished hippocampal CA1 cell loss and preserved long-term potentiation expression. The neuroprotective effect was robust in the event of pretreatment, and also when the drug was administered at the time of reperfusion.

A detailed analysis of the behavioral effects of this new compound appeared to be extremely important, and we have therefore investigated it from several aspects.

In a preliminary investigation of the effects of the analog on mice, we performed open-field tests of the locomotor activity and exploratory drive. The influence of the analog on spatial orientation and learning was also assessed in the radial arm maze imprinting test. In the Morris water maze tests we examined its effects on the working memory and long-lasting reference memory of rats.

It emerged that there is a dose of this KYNA-amide which is neuroprotective, but does not worsen the cognitive function of the brain. This result is significant in that a putative neuroprotectant without adverse cognitive side-effects is of great benefit.

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Developmental regulation of brassinosteroid distribution in *Arabidopsis*

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Brassinosteroids (BRs; steroidal phytohormones) are essential regulators of plant growth and development. Unlike most other hormones, BRs are not subject to active transport, but exert their effects locally, in a paracrine manner. Local BR levels are efficiently controlled by the coordinated actions of biosynthetic and degradative gene functions, which ensure both homeostatic and differential regulation. While the transcriptional regulation of BR biosynthetic genes is known in great detail, its direct effects on the hormone production and accumulation are still to be clarified.

The aim of our study is to find out how castasterone and brassionolide, the two biologically active forms of BRs, are distributed in the model plant *Arabidopsis thaliana*. To observe developmental changes in the hormone accumulation, we generated transgenic plants expressing reporter genes under the control of an artificial BR-responsive promoter. The BR response constructs will be used for monitoring developmental BR adjustments during morphogenic events, such as germination and the differentiation of reproductive organs. Parallelly, we determine the bioactive BRs in all *Arabidopsis* organs via CG-MS analyses, in order to construct a comprehensive map of hormone distribution in the adult plant. In another approach, we initiated studies on the role of regulated hormone distribution during embryonic development. This line of research utilizes GFP and LUC reporter-tagged versions of the CYP85A2 enzyme that catalyzes the rate-limiting step of BR biosynthesis. The transgenic lines expressing these chimeric proteins will be helpful in elucidating the induction and spatial pattern of embryonic BR synthesis, and its correlation with the developmental auxin re-distribution that has been well characterized.

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The examination of the telomer protecting *Drosophila melanogaster* gene (*dtl*)

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In *Drosophila melanogaster* chromosome ends consist of retrotransposon arrays, the well-defined, short telomeric repeats, characteristic of human and other telomerase-containing organisms are absent. Consequently, in Drosophila there is no need for the sequence-specific,